IN THE CLAIMS:

Claim\1 (previously amended): An amide derivative of the Formula I

Q $(R^2)_p$ H $(CH_2)_q$ R^4 I

wherein

R³ is (1-6C)alkyl or halogeno;

O is phenyl or naphthyl which optionally bears 1, 2, 3 or 4 substituents selected from hydroxy, halogeno, trifluoromethyl\cyano, mercapto, nitro, amino, carboxy, carbamoyl, formyl, (1-6C)alkyl, (2-6C)alkenyl, (2-6C)alkynyl, (1-6C)alkoxy, (1-3C)alkylenedioxy, (1-6C)alkylthio, (1-6C)alkylsulphin \(\), (1-6C)alkylsulphonyl, (1-6C)alkylamino, di-[(1-6C)alkyl]amino, (1-6C)alkoxycarbonyl, N-(1-6C)alkylcarbamoyl, N,N-di-[(1-6C)alkyl]carbamoyl, (2-6C)alkanoyl, (2-6C)alkanoyloxy, (1-6C)alkanoylamino, N-(1-6C)alkylsulphamoyl, N,N-di-[(1-6C)alkyl]sulphamoyl, (1-6C)alkanesulphonylamino, N-(1-6C)alkyl-(1-6C)alkanesulphonylamino, halogeno-(1-6C)alkyl, hydroxy-(1-6C)alkyl, (146C)alkoxy-(1-6C)alkyl, cyano-(1-6C)alkyl, amino-(1-6C)alkyl, (1-6C)alkylamino-(1-6C)alkyl, di-[(1-6C)alkyl]amino-(1-6C)alkyl, carboxy-(1-6C)alkyl, (1-6C)alkoxycarbonyl-(1-6C)alkyl, carbamoyl-(1-6C)alkyl, N-(1-6C)alkylcarbamoyl-(1-6C)alkyl, N,N-di-[(1-6C)alkyl]carbamoyl-(1-6C)alkyl, halogeno-(2-6C)alkoxy, hydroxy-(2-6C)alkoxy, (1-6C)alkoxy-(2-6C)alkoxy, cyano-(1-6C)alkoxy, carboxy-(1-6C)alkoxy, (1-6C)alkoxycarbonyl-(1-6C)alkoxy, carbamoyl-(1-6C)alkoxy, N-(1-6C)alkylcarbamoyl-(1-6C)alkoxy, N,N-di-[(1-6C)alkyl]carbamoyl-(1-6C)alkoxy, amino-(2-6C)alkoxy,

50h

(1-6C)alkylamino-(2-6C)alkoxy, di-[(1-6C)alkyl]amino-(2-6C)alkoxy,

halogeno-(2-6C)alkylamino, hydroxy-(2-6C)alkylamino,

(1-6C)alkylamino, cyano-(1-6C)alkylamino, carboxy-(1-6C)alkylamino,

(1-6C)alkoxycarbonyl-(1-6C)alkylamino, carbamoyl-(1-6C)alkylamino,

N-(1-6C)alkylcarbamoyl-(1-6C)alkylamino,

 $\underline{N},\underline{N}$ -di-[(1- δC)alkyl]carbamoyl-(1- δC)alkylamino, amino-(2- δC)alkylamino,

(1-6C)alkylamino-(2-6C)alkylamino, di-[(1-6C)alkyl]amino-(2-6C)alkylamino,

 \underline{N} -(1-6C)alkyl-halogeno-(1-6C)alkylamino, \underline{N} -(1-6C)alkyl-hydroxy-(2-6C)alkylamino,

N-(1-6C)alkyl-(1-6C)alkoxy-(2-6C)alkylamino,

 \underline{N} -(1-6C)alkyl-cyano $\frac{1}{6}$ (1-6C)alkylamino, \underline{N} -(1-6C)alkyl-carboxy-(1-6C)alkylamino,

 \underline{N} -(1-6C)alkyl-(1-6C)alkylamino, \underline{N} -(1-6C)alkyl-carbamoyl-

(1-6C)alkylamino, N-(1-6C)alkyl-N-(1-6C)alkylcarbamoyl-(1-6C)alkylamino,

 \underline{N} -(1-6C)alkyl- \underline{N} , \underline{N} -di-[(1- δ C)alkyl]carbamoyl-(1-6C)alkylamino,

N-(1-6C)alkyl-amino-(2-6C)alkylamino, N-(1-6C)alkyl-(1-6C)alkylamino-

(2-6C)alkylamino, N-(1-6C)alkyl-di-[(1-6C)alkyl]amino-(2-6C)alkylamino,

halogeno-(2-6C)alkanoylamino, hydroxy-(2-6C)alkanoylamino,

(1-6C)alkoxy-(2-6C)alkanoylamino, cyano-(2-6C)alkanoylamino,

carboxy-(2-6C)alkanoylamino, (1-6C)alkoxycarbonyl-(2-6C)alkanoylamino,

carbamoyl-(2-6C)alkanoylamino, N-(1-6C)alkylcarbamoyl-(2-6C)alkanoylamino,

N,N-di-[(1-6C)alkyl]carbamoyl-(2-6C)alkanoylamino, amino-(2-6C)alkanoylamino,

(1-6C)alkylamino-(2-6C)alkanoylamino, di-[(1-6C)alkyl]amino-(2-6C)alkanoylamino,

aryl, aryl-(1-6C)alkyl, aryl-(1-6C)alkoxy, arylamino,

N-(1-6C)alkyl-arylamino, aryl-(1-6C)alkylamino,

N-(1-6C)alkyl-aryl-(1-6C)alkylamino, aroylamino, arylsulphonylamino,

N-arylsulphamoyl, aryl-(2-6C)alkanoylamino, heteroaryl, heteroaryl-(1-6C)alkyl,

heteroaryloxy, heteroaryl-(1-6C)alkoxy, heteroarylamino,

N-(1-6C)alkyl-heteroarylamino, heteroaryl-(1-6C)alkylamino,

N-(1-6C)alkyl-heteroaryl-(1-6C)alkylamino, heteroarylcarbonylamino,

 $heteroaryl sulphonylamino, \underline{N}-heteroaryl sulphamoyl, heteroaryl-(2-6C) alkanoylamino, \\$

heterocyclyl, heterocyclyl-(1-6C)alkyl, heterocyclyloxy, heterocyclyl-(1-6C)alkoxy,

1-WA/1973526.1

509

Page 4

heterocyclylamino, \underline{N} -(1-6C)alkyl-heterocyclylamino, heterocyclyl-(1-6C)alkylamino, \underline{N} -(1-6C)alkyl-heterocyclyl-(1-6C)alkylamino, heterocyclylcarbonylamino, heterocyclylsulphonylamino, \underline{N} -heterocyclylsulphamoyl and heterocyclyl-(2-6C)alkanoylamino,

and wherein any of the substituents on Q defined hereinbefore which comprise a CH₂ group which is attached to 2 carbon atoms or a CH₃ group which is attached to a carbon atom may optionally bear on each said CH₂ or CH₃ group a substituent selected from hydroxy, amino, (1-6C)alkoxy, (1-6C)alkylamino, di-[(1-6C)alkyl]amino and heterocyclyl;

and wherein any aryl, heteroaryl or heterocyclyl group in a substituent on Q may optionally bear 1 or 2 substituents selected from hydroxy, halogeno, (1-6C)alkyl, (1-6C)alkoxy, carboxy, (1-6C)alkoxycarbonyl, N-(1-6C)alkylcarbamoyl, N-(1-6C)alkylcarbamoyl, (2-6C)alkanoyl, amino, (1-6C)alkylamino, di-[(1-6C)alkyl]amino, halogeno-(1-6C)alkyl, hydroxy-(1-6C)alkyl, (1-6C)alkoxy-(1-6C)alkyl, cyano-(1-6C)alkyl, amino-(1-6C)alkyl, (1-6C)alkylamino-(1-6C)alkyl, di-[(1-6C)alkyl]amino-(1-6C)alkyl, aryl and aryl-(1-6C)alkyl;

R² is hydroxy, halogeno, trifluoromethyl, cyano, mercapto, nitro, amino, carboxy, (1-6C)alkoxycarbonyl, (1-6C)alkyl, (2-6C)alkenyl, (2-6C)alkynyl, (1-6C)alkoxy, (1-6C)alkylamino or di-[(1-6C)alkyl]amino;

p is 0, 1 or 2;

q is 0, 1, 2, 3 or 4; and

R⁴ is aryl, aryl-(1-6C)alkoxy, aryloxy, <u>N</u>-(1-6C)alkyl-arylamino, aryl-(1-6C)alkylamino, <u>N</u>-(1-6C)alkyl-aryl-(1-6C)alkylamino, aroylamino, arylsulphonylamino, <u>N</u>-arylsulphamoyl, aryl-(2-6C)alkanoylamino, cycloalkyl, heteroaryl, heteroaryloxy, heteroaryl-(1-6C)alkoxy, heteroarylamino, <u>N</u>-(1-6C)alkyl-heteroarylamino, heteroaryl-(1-6C)alkyl-heteroaryl-(1-6C)alkylamino, heteroarylsulphonylamino, <u>N</u>-heteroarylsulphamoyl, heteroaryl-(2-6C)alkanoylamino, heterocyclyl, heterocyclyloxy, heterocyclyl-(1-6C)alkoxy, heterocyclylamino, <u>N</u>-(1-6C)alkyl-heterocyclylamino, heterocyclyl-(1-6C)alkylamino,

Page 5

 \underline{N} -(1-6C)alkyl-heterocyclyl-(1-6C)alkylamino, heterocyclylcarbonylamino,

heterocyclylsulphonylamino, N-heterocyclylsulphamoyl or

heterocyclyl-(2-6C)alkanoylamino and R⁴ optionally bears 1, 2, 3 or 4 substituents selected from

hydroxy, halogeno, trifluoromethyl, cyano, mercapto, nitro, amino, carboxy, carbamoyl,

formyl, (1-6C)alkyl, (2-6C)alkenyl, (2-6C)alkynyl, (1-6C)alkoxy, (1-3C)alkylenedioxy,

(1-6C)alkylthid, (1-6C)alkylsulphinyl, (1-6C)alkylsulphonyl, (1-6C)alkylamino,

di-[(1-6C)alkyl]amino, (1-6C)alkoxycarbonyl, N-(1-6C)alkylcarbamoyl,

N,N-di-[(1-6C)alky\carbamoyl, (2-6C)alkanoyl, (2-6C)alkanoyloxy,

(1-6C)alkanoylamino, $\underline{\mathbb{V}}$ -(1-6C)alkylsulphamoyl, $\underline{\mathbb{N}}$ -di-[(1-6C)alkyl]sulphamoyl,

(1-6C)alkanesulphonylamino, N-(1-6C)alkyl-(1-6C)alkanesulphonylamino,

halogeno-(1-6C)alkyl, hydroxy-(1-6C)alkyl, (1-6C)alkoxy-(1-6C)alkyl,

cyano-(1-6C)alkyl, amino-(1\6C)alkyl, (1-6C)alkylamino-(1-6C)alkyl,

di-[(1-6C)alkyl]amino-(1-6C)alkyl, carboxy-(1-6C)alkyl,

(1-6C)alkoxycarbonyl-(1-6C)alkyl, carbamoyl-(1-6C)alkyl,

 \underline{N} -(1-6C)alkylcarbamoyl-(1-6C)alk χ l, \underline{N} -di-[(1-6C)alkyl]carbamoyl-(1-6C)alkyl,

halogeno-(2-6C)alkoxy, hydroxy-(2-6C)alkoxy, (1-6C)alkoxy-(2-6C)alkoxy,

cyano-(1-6C)alkoxy, carboxy-(1-6C)alkoxy, (1-6C)alkoxycarbonyl-(1-6C)alkoxy,

carbamoyl-(1-6C)alkoxy, N-(1-6C)alkylcarbamoyl-(1-6C)alkoxy,

 $\underline{N},\underline{N}$ -di-[(1-6C)alkyl]carbamoyl-(1-6C)alkoxy, amino-(2-6C)alkoxy,

(1-6C)alkylamino-(2-6C)alkoxy, di-[(1-6C)alkyl]amino-(2-6C)alkoxy,

halogeno-(2-6C)alkylamino, hydroxy-(2-6C)alkylamino,

(1-6C)alkoxy-(2-6C)alkylamino, cyano-(1-6C)alkylamino, carboxy-(1-6C)alkylamino,

(1-6C)alkoxycarbonyl-(1-6C)alkylamino, carbamdyl-(1-6C)alkylamino,

N-(1-6C)alkylcarbamoyl-(1-6C)alkylamino,

N,N-di-[(1-6C)alkyl]carbamoyl-(1-6C)alkylamino, amino-(2-6C)alkylamino,

(1-6C)alkylamino-(2-6C)alkylamino, di-[(1-6C)alkyl]amino-(2-6C)alkylamino,

 \underline{N} -(1-6C)alkyl-halogeno-(1-6C)alkylamino, \underline{N} -(1-6C)alkyl-hydroxy-(2-6C)alkylamino,

N-(1-6C)alkyl-(1-6C)alkoxy-(2-6C)alkylamino,

 \underline{N} -(1-6C)alkyl-cyano-(1-6C)alkylamino, \underline{N} -(1-6C)alkyl-carboxy-(1-6C)alkylamino,

5.b

Page 6

d'

ζυh

N-(1-6C)alkyl-(1-6C)alkoxycarbonyl-(1-6C)alkylamino, N-(1-6C)alkyl-carbamoyl-(1-6C)alkylamino, N-(1-6C)alkyl-N-(1-6C)alkylcarbamoyl-(1-6C)alkylamino, N-(1-6C)alkyl-N,N-di-[(1-6C)alkyl]carbamoyl-(1-6C)alkylamino, N-(1-6C)alkyl-amino-(2-6C)alkylamino, N-(1-6C)alkyl-(1-6C)alkylamino-

(2-6C)alkylamino, N-(1-6C)alkyl-di-[(1-6C)alkyl]amino-(2-6C)alkylamino,

halogeno-(2-6C)alkanoylamino, hydroxy-(2-6C)alkanoylamino,

(1-6C)alkoxy-(2-6C)alkanoylamino, cyano-(2-6C)alkanoylamino,

carboxy-(2-6C)alkanoylamino, (1-6C)alkoxycarbonyl-(2-6C)alkanoylamino,

carbamoyl-(2-6C)alkanoylamino, N-(1-6C)alkylcarbamoyl-(2-6C)alkanoylamino,

N,N-di-[(1-6C)alkyl]carbamoyl-(2-6C)alkanoylamino, amino-(2-6C)alkanoylamino,

(1-6C)alkylamino-(2-6C)alkanoylamino, di-[(1-6C)alkyl]amino-(2-6C)alkanoylamino,

aryl, aryl-(1-6C)alkyl, aryl-(1-6C)alkoxy, aryloxy, arylamino, N-(1-6C)alkyl-arylamino, aryl-(1-6C)alkylamino,

N-(1-6C)alkyl-aryl-(1-6C)alkylamino, aroylamino, arylsulphonylamino,

N-arylsulphamoyl, aryl-(2-6C)alkanoylamino, heteroaryl, heteroaryl-(1-6C)alkyl,

heteroaryloxy, heteroaryl-(1-6C)alkoxy, heteroarylamino,

N-(1-6C)alkyl-heteroarylamino, heteroaryl-(1-6C)alkylamino,

N-(1-6C)alkyl-heteroaryl-(1-6C)alkylamino, heteroarylcarbonylamino,

heteroarylsulphonylamino, N-heteroarylsulphamoyl, heteroaryl-(2-6C)alkanoylamino,

heterocyclyl, heterocyclyl-(1-6C)alkyl, heterocyclyloxy, heterocyclyl-(1-6C)alkoxy,

heterocyclylamino, N-(1-6C) alkyl-heterocyclylamino, heterocyclyl-(1-6C) alkylamino,

N-(1-6C)alkyl-heterocyclyl-(1-6C)alkylamino, heterocyclylcarbonylamino,

eterocyclylsulphonylamino, N-heterocyclylsulphamoyl and

heterocyclyl-(2-6C)alkanoylamino,

and wherein any of the substituents on R⁴ defined hereinbefore which comprise a CH₂ group which is attached to 2 carbon atoms or a CH₃ group which is attached to a carbon atom may optionally bear on each said CH₂ or CH₃ group a substituent selected from hydroxy, amino, (1-6C)alkoxy, (1-6C)alkylamino, di-[(1-6C)alkyl]amino and heterocyclyl;

Page 7

and wherein any aryl, heteroaryl or heterocyclyl group in a substituent on R⁴ may optionally bear 1 or 2 substituents selected from hydroxy, halogeno, (1-6C)alkyl, (1-6C)alkoxy, carboxy, (1-6C)alkoxycarbonyl, N-(1-6C)alkylcarbamoyl, N-(1-6C)alkylcarbamoyl, (2-6C)alkanoyl, amino, (1-6C)alkylamino, di-[(1-6C)alkyl]amino, halogeno-(1-6C)alkyl, hydroxy-(1-6C)alkyl, (1-6C)alkoxy-(1-6C)alkyl, cyano-(1-6C)alkyl, amino-(1-6C)alkyl, (1-6C)alkylamino-(1-6C)alkyl, di-[(1-6C)alkyl]amino-(1-6C)alkyl, aryl and aryl-(1-6C)alkyl;

or a pharmaceutically-acceptable salt or <u>in-vivo</u>-cleavable ester thereof; except that the compounds:-

N-(2-cyclohexylethyl)-3\(4-hydroxybenzamido)-4-methylbenzamide,

 $3-(4-aminobenzamido)-\underline{N}-(4-carboxy-3-hydroxyphenyl)-4-methylbenzamide,$

N-(4-carboxy-3-hydroxyphenyl)-4-methyl-3-(4-nitrobenzamido)benzamide,

3-(4-aminobenzamido)-4-methyl-N-(2-pyridyl)benzamide,

4-methyl-3-(4-nitrobenzamido) \N-(2-pyridyl)benzamide,

3-(4-aminobenzamido)-4-methyl-\(\frac{\pi}{2}\)-(2-thiazolyl)benzamide,

4-methyl-3-(4-nitrobenzamido)-N-(2-thiazolyl)benzamide,

3-benzamido-4-chloro-N-(2-fluoroan lino) benzamide,

3-(2-hydroxy-4-methylbenzamido)-N-(4-hydroxyphenyl)-4-methylbenzamide,

 $3-(3-hydroxy-2-naphthoylamino)-4-methyl-\underline{N}-phenylbenzamide and$

4-chloro-3-(3-hydroxy-2-naphthoylamino) 2-methyl-N-phenylbenzamide are excluded.

Claim 2 (previously amended): An amide derivative of the Formula I according to claim 1 wherein

R³ is methyl, ethyl, chloro or bromo;

Q is phenyl which bears 1, 2 or 3 substituents selected from hydroxy, fluoro, chloro, trifluoromethyl, cyano, carboxy, methyl, ethyl, propyl, methoxy, ethoxy, methylenedioxy, methoxycarbonyl, ethoxycarbonyl, tert-butoxycarbonyl, acetyl, propionyl, chloromethyl, methoxymethyl, methylaminomethyl, ethylaminomethyl, diethylaminomethyl, 2-chloroethoxy, 3-chloropropoxy, 2-

6.h

d'

Sub

hydroxyethoxy, 3-hydroxypropoxy, 2-methoxyethoxy, 2-ethoxyethoxy, 3-methoxypropoxy, 3-ethoxypropoxy, cyanomethoxy, carboxymethoxy, methoxycarbonylmethoxy, ethoxycarbonylmethoxy, tert-butoxycarbonylmethoxy, 2-aminoethoxy, 3-aminopropoxy, 2-methylaminoethoxy, 2-ethylaminoethoxy, 3-methylaminopropoxy, 3-ethylaminopropoxy, 2-dimethylaminopropoxy, 2-dimethylaminopropoxy, 3-dimethylaminopropoxy, 3-diethylaminopropoxy, 2-pyridylmethoxy, 2-(imidazol-1-yl)ethoxy, 3-(imidazol-1-yl)propoxy, pyrrolidin-1-yl, piperidino, morpholino, piperazin-1-yl, 4-methylpiperazin-1-yl, 4-acetylpiperazin-1-ylnethyl, 4-methylpiperazin-1-ylmethyl, piperidinomethyl, morpholinomethyl, piperidin-4-yloxy, 1-methylpiperazin-1-ylmethyl, 4-acetylpiperazin-1-yllmethyl, 4-piperidinopropoxy, 2-piperidinoethoxy, 3-piperidinopropoxy, 2-morpholinoethoxy, 3-morpholinopropoxy, 2-piperazin-1-ylethoxy, 3-piperazin-1-ylpropoxy, 2-(4-methylpiperazin-1-yl)pthoxy, 3-(4-methylpiperazin-1-yl)propoxy, 2-(4-acetylpiperazin-1-yl)ethoxy, and 3-(4-acetylpiperazin-1-yl)propoxy;

p is 0;

q is 0; and

R⁴ is phenyl which bears 1 or 2 substituents selected from hydroxy, fluoro, chloro, trifluoromethyl, cyano, amino, methyl, ethyl, methoxy, ethoxy, methylenedioxy, methylamino, ethylamino, dimethylamino, diethylamino, acetyl, propionyl, chloromethyl, methoxymethyl, 2-methoxyethyl, methylaminomethyl, ethylaminomethyl, dimethylaminomethyl, diethylaminomethyl, 2-chloroethoxy, 3-chloropropoxy, 2-hydroxyethoxy, 3-hydroxypropoxy, 2-methoxyethoxy, 2-ethoxyethoxy, 3-methoxypropoxy, 3-ethoxypropoxy, cyanomethoxy, carboxymethoxy, methoxycarbonylmethoxy, ethoxycarbonylmethoxy, tert-butoxycarbonylmethoxy, 2-aminoethoxy, 3-aminopropoxy, 2-methylaminoethoxy, 2-ethylaminoethoxy, 3-methylaminopropoxy, 3-diethylaminopropoxy, 2-diethylaminopropoxy, 2-chloroethylamino, 2-hydroxyethylamino, 2-methylamino, 2-methylamino, 2-ethoxyethylamino, 2-ethoxyethylamino, 2-aminoethylamino, 2-methylaminoethylamino, 2-ethylaminoethylamino,

Page 9

2-dimethylamino, 2-diethylamino thylamino, \underline{N} -(2-chloroethyl)- \underline{N} -methylamino, \underline{N} -(2-hydroxyethyl)- \underline{N} -methylamino, \underline{N} -(2-methoxyethyl)- \underline{N} -methylamino, \underline{N} -(2-aminoethyl)- \underline{N} -methylamino,

N-(2-methylaminoethyl)-N-methylamino, N-(2-dimethylaminoethyl)-N-methylamino,

 \underline{N} -(3-aminopropyl)- \underline{N} -methylamino, \underline{N} -(3-methylaminopropyl)- \underline{N} -methylamino,

 \underline{N} -(3-ethylaminopropyl)- \underline{N} -methylamino, \underline{N} -(3-dimethylaminopropyl)- \underline{N} -methylamino,

 \underline{N} -(3-diethylamino, phenyl, benzyl, benzyloxy,

2-pyridylmethoxy, 2-(imidazol-1-yl)ethoxy, 3-(imidazol-1-yl)propoxy, pyrrolidin-1-yl, piperidino, morpholino, piperazin-1-yl, 4-methylpiperazin-1-yl, 4-acetylpiperazin-1-yl, pyrrolidin-1-ylmethyl, piperidinomethyl, morpholinomethyl, piperazin-1-ylmethyl, 4-acetylpiperazin-1-ylmethyl, piperidin-4-yloxy,

1-methylpiperidin-4-yloxy, 2-(pyrrolidin-1-yl)ethoxy,

3-(pyrrolidin-1-yl)propoxy, 2-piperidinoethoxy, 3-piperidinopropoxy,

2-morpholinoethoxy, 3-morpholinopropoxy, 2-piperazin-1-ylethoxy,

3-piperazin-1-ylpropoxy, 2-(4-methylpiperazin-1-yl)ethoxy,

3-(4-methylpiperazin-1-yl)propoxy, 2-(4-acetylpiperazin-1-yl)ethoxy and

3-(4-acetylpiperazin-1-yl)propoxy;

or a pharmaceutically-acceptable salt thereof;

except that 3-(2-hydroxy-4-methylbenzamido)-<u>N</u>-(4-hydroxyphenyl)-4-methylbenzamide is excluded.

Claim 3 (original, reformatted): An amide derivative of the Formula I according to claim 1 wherein

R³ is methyl or chloro;

Q is phenyl which bears 1, 2 or 3 substituents selected from hydroxy, cyano, carboxy, methyl, ethyl, propyl, methoxy, ethoxy, acetyl and 2-methoxyethoxy;

p is 0;

q is 0; and

R⁴ is phenyl which bears 1 or 2 substituents selected from chloro, cyano and dimethylamino; or a pharmaceutically-acceptable salt thereof.

Sub

ATTORNEY DOCKET NO.: 056291-5055

Application No.: 09/762,106

Page 10

Claim 4 (cancelled).

Claim 5 (original): An amide derivative of the Formula I according to claim 1 wherein Q is substituted by a basic substituent selected from the substituents for Q defined in claim 1 and R⁴ is a phenyl or heteroaryl group as defined in claim 1 which also bears a basic substituent selected from the substituents for R⁴ defined in claim 1.

Claim 6 (original, reformatted): An amide derivative of the Formula I according to claim 1 wherein

R³ is methyl or chloro;

Q is phenyl which bears a substituent selected from dimethylaminomethyl, diethylaminomethyl, N-butyl-N-methylaminomethyl, 2-dimethylaminoethoxy, 2-diethylaminoethoxy, 2-diisopropylaminoethoxy, 3-dimethylaminopropoxy, 3-diethylaminopropoxy, 3-diisopropylaminopropoxy, pyrrolidin-1-ylmethyl, 3-hydroxypyrrolidin-1-ylmethyl, morpholinomethyl, piperidinomethyl, homopiperidinomethyl, piperazin-1-ylmethyl, homopiperazin-1-ylmethyl, 4methylpiperazin-1-ylmethyl, 4-methylhomopiperazin-1-ylmethyl, 4-ethylpiperazin-1ylmethyl, 4-ethylhomopiperazin-1-ylmethyl, 4-isopropylpiperazin-1-ylmethyl, 4-(2-hydroxyethyl)piperazin-1-ylmethyl, 2 pyridylmethoxy, pyrrolidin-3-yloxy, 1-methylpyrrolidin-3-yloxy, piperidin-3-yloxy, 1-methylpiperidin-3-yloxy, homopiperidin-3-yloxy, 1-methylhomopiperidin-3-yloxy, piperidin-4-yloxy, 1methylpiperidin-4-yloxy, homopiperidin-4-yloxy, 1-methylhomopiperidin-4-yloxy, pyrrolidin-3-ylmethoxy, 1-methylpyrrolidin-3-ylmethoxy, piperidin-3-ylmethoxy, 1methylpiperidin-3-ylmethoxy, homopiperidin-3-ylmethoxy, 1-methylhomopiperidin-3vlmethoxy, piperidin-4-ylmethoxy, 1-methylpiperidin-4-ylmethoxy, homopiperidin-4ylmethoxy, 1-methylhomopiperidin-4-ylmethoxy, 2-(pyrròllidin-1-yl)ethoxy, 3-(pyrrolidin-1-yl)propoxy, 2-(N-methylpyrrolidin-2-yl)ethoxy, 3-(N-methylpyrrolidin-2yl)propoxy, 2-piperidinoethoxy, 3-piperidinopropoxy, 2-morpholinoethoxy, 3-

ATTORNEY DOCKET NO.: 056291-5055

Application No.: 09/762,106

Page 11

morpholinopropoxy, 2-piperazin-1-ylethoxy, 2-homopiperazin-1-ylethoxy, 3-piperazin-1-ylpropoxy, 3-homopiperazin-1-ylpropoxy, 2-(4-methylpiperazin-1-yl)ethoxy, 2-(4-methylhomopiperazin-1-yl)ethoxy, 3-(4-methylhomopiperazin-1-yl)propoxy, 2-(4-acetylpiperazin-1-yl)ethoxy, 3-(4-acetylpiperazin-1-yl)propoxy, 2-methoxyethylaminomethyl, 3-methoxypropylaminomethyl, 2-aminoethylaminomethyl, 3-aminopropylaminomethyl, 2-dimethylaminoethylaminomethyl, 3-methylaminopropylaminomethyl, 2-dimethylaminoethylaminomethyl, 3-methylaminopropylaminomethyl, 2-dimethylaminoethylaminomethyl, 3-dimethylaminopropylaminomethyl, N-(2-methylaminoethyl)-N-methylaminomethyl, N-(3-methylaminopropyl)-N-methylaminomethyl, N-(2-dimethylaminomethyl)-N-methylaminomethyl, N-(3-dimethylaminopropyl)-N-methylaminomethyl and 3-morpholinopropylaminomethyl, and Q is optionally substituted with a further substituent selected from methyl and methoxy;

p is 0;

q is 0; and

R⁴ is phenyl which is substituted at the 3-position with a substituent selected from dimethylamino, diethylamino, pyrrolidin-1-yl, piperidino, morpholino, piperazin-1-yl, homopiperazin-1-yl, 4-methylpiperazin-1-yl and 4-methylhomopiperazin-1-yl and R⁴ is optionally substituted with a further substituent selected from fluoro, chloro, cyano, methyl and trifluoromethyl;

or a pharmaceutically-acceptable salt thereof.

Claim 7 (cancelled).

Claim 8 (previously amended): An amide derivative of the Formula I according to claim 1 selected from :-

N-(3-dimethylaminophenyl)-4-methyl-3-(4-propylbenzamido) benzamide,

3-(3,4-dimethoxybenzamido)-N-(3-dimethylaminophenyl)-4-methylbenzamide,

 $3-(4-butoxybenzamido)-\underline{N}-(3-dimethylaminophenyl)-4-methylbenzamide,$

4-chloro-N-(3-dimethylaminophenyl)-3-(4-propylbenzamido)benzamide,

,

3-(4-carboxybenzamido)-N-(3-dimethylaminophenyl)-4-methylbenzamide,

 \underline{N} -(3,4\dichlorobenzyl)-3-(3,4,5-trimethoxybenzamido)-4-methylbenzamide,

N-(2-cyclohexylethyl)-3-(3,4-dimethoxybenzamido)-4-methylbenzamide,

4-methyl-N₃(3-morpholinophenyl)-3-(3-piperidin-4-yloxybenzamido)benzamide,

4-chloro-N-(3-fluoro-5-morpholinophenyl)-3-[3-(1-methylhomopiperidin-4-yloxy)benzamido]benzamide,

3-(2-diisopropylaminoethoxybenzamido)-4-methyl-N-(3-morpholinophenyl)benzamide,

3-(4-diethylaminomethylbenzamido)-4-methyl-N-(3-morpholinophenyl)benzamide,

4-methyl-3-[3-(4-methylhomopiperazin-1-ylmethyl)benzamido]-<u>N</u>-(3-morpholinophenyl)-benzamide, and

4-methyl-3-[3-(4-methylpiperazin-1-ylmethyl)benzamido]-<u>N</u>-(3-morpholinophenyl)-benzamide;

or a pharmaceutically-acceptable salt thereof.

Claim 9 (original, reformatted): A process for the preparation of an amide derivative of the Formula I, or a pharmaceutically-acceptable salt or <u>in-vivo</u>-cleavable ester thereof, according to claim 1 which comprises:-

(a) reacting a benzoic acid of the Formula II, or a reactive derivative thereof,

with an amine of the Formula III

$$H_2N \longrightarrow (CH_2)_q \longrightarrow R^4$$
 III

under standard amide bond forming conditions, wherein variable groups are as defined in claim 1 and wherein any functional group is protected if necessary, and:

- (i) removing any protecting groups; and
- (ii) optionally forming a pharmaceutically-acceptable salt or <u>in-vivo</u>-cleavable ester;

¢'

50

Page 13

(b) reacting an acid of the Formula IV, or an activated derivative thereof,

with an aniline of the Formula VI

$$R^3$$
 $(R^2)_p$
 H_2N
 O
 $(CH_2)_q$
 R^4
 VI

under standard amide bond forming conditions as defined hereinbefore, wherein variable groups are as defined in claim 1 and wherein any functional group is protected, if necessary, and:

- (i) removing any protecting groups;
- (ii) optionally forming a pharmaceutically-acceptable salt or in-vivo-cleavable ester;
- (c) for the preparation of a compound of the Formula I wherein a substituent on Q or R⁴ is (1-6C)alkoxy or substituted (1-6C)alkoxy, (1-6C)alkylthio, (1-6C)alkylamino, di-[(1-6C)alkyl]amino or substituted (1-6C)alkylamino or heterocyclyloxy, the alkylation, conveniently in the presence of a suitable base, of an amide derivative of the Formula I wherein a substituent on Q or R⁴ is hydroxy, mercapto or amino as appropriate;
- (d) for the preparation of a compound of the Formula I wherein a substituent on Q or R⁴ is (1-6C)alkanoylamino or substituted (2-6C)alkanoylamino, the acylation of a compound of the Formula I wherein a substituent on Q or R⁴ is amino;
- (e) for the preparation of a compound of the Formula I wherein a substituent on Q or R⁴ is (1-6C)alkanesulphonylamino, the reaction of a compound of the Formula I wherein a substituent on Q or R⁴ is amino with a (1-6C)alkanesulphonic acid, or an activated derivative thereof;
- (f) for the preparation of a compound of the Formula I wherein a substituent on Q or R⁴

. ران

age 14

is carboxy, carboxy-(1-6C)alkyl, carboxy-(1-6C)alkoxy, carboxy-(1-6C)alkylamino, N-(1-6C)alkyl-carboxy-(1-6C)alkylamino or carboxy-(2-6C)alkanoylamino, the cleavage of a compound of the Formula I wherein a substituent on Q or R⁴ is (1-6C)alkoxycarbonyl, (1-6C)alkoxycarbonyl-(1-6C)alkyl, (1-6C)alkoxycarbonyl-(1-6C)alkylamino, N-(1-6C)alkyl-(1-6C)alkoxycarbonyl-(1-6C)alkylamino, N-(1-6C)alkyl-(1-6C)alkoxycarbonyl-(1-6C)alkylamino or (1-6C)alkoxycarbonyl-(2-6C)alkanoylamino as appropriate;

- (g) for the preparation of a compound of the Formula I wherein a substituent on Q or R⁴ is amino-(1-6C)alkyl, heterocyclyl-(1-6C)alkyl, (1-6C)alkylamino-(1-6C)alkyl, di-[(1-6C)alkyl]amino-(1-6C)alkyl, substituted (2-6C)alkylamino-(1-6C)alkyl or substituted N-(1-6C)alkyl-(2-6C)alkylamino-(1-6C)alkyl, the reaction of a compound of the Formula I wherein a substituent on Q or R⁴ is a group of the formula -(1-6C)alkylene-Z wherein Z is a displaceable group with an appropriate amine or heterocyclyl compound;
- (h) for the preparation of a compound of the Formula I wherein a substituent on Q or R⁴ is amino, heterocyclyl, (1-6C)alkylamino, di-[(1-6C)alkyl]amino, substituted (1-6C)alkylamino, substituted N-(1-6C)alkyl-(1-6C)alkylamino, substituted (2-6C)alkylamino or substituted N-(1-6C)alkyl-(2-6C)alkylamino, the reaction of a compound of the Formula I wherein a substituent on Q or R⁴ is a displaceable group Z with an appropriate amine or heterocyclyl compound;
- (i) for the preparation of a compound of the Formula I wherein a substituent on Q or R⁴ is N-(1-6C)alkyl-(1-6C)alkanesulphonylamino, the alkylation, conveniently in the presence of a suitable base, of an amide derivative of the Formula I wherein a substituent on Q or R⁴ is (1-6C)alkanesulphonylamino;
- (j) for the preparation of a compound of the Formula I wherein a substituent on Q or R⁴ is a hydroxy-heterocyclyl-(1-6C)alkoxy group, a hydroxy-(1-6C)alkylamino-(2-6C)alkoxy group or a hydroxy-di-[(1-6C)alkyl]amino-(2-6C)alkoxy group, the reaction of a compound of the Formula I wherein a substituent on Q or R⁴ is a epoxy-substituted (1-6C)alkoxy group with a heterocyclyl compound or an appropriate amine; or

50h

ATTORNEY DOCKET NO.: 056291-5055

Application No.: 09/762,106

Page 15

(k) for the preparation of a compound of the Formula I wherein R² or a substituent on Q or R⁴ is an amino group, the reduction of a compound of the Formula I wherein R² or a substituent on Q or R⁴ is a nitro group.

Claim 10 (original): A pharmaceutical composition which comprises an amide derivative of the Formula I, or a pharmaceutically-acceptable or <u>in-vivo</u>-cleavable ester thereof, according to claim 1 in association with a pharmaceutically-acceptable diluent or carrier.

Claim 11 (cancelled).

Claim 12 (currently amended): A method for treating a disease or medical condition mediated by the production or effect of a cytokine TNF, said method comprising administering to a warm-blooded animal in need thereof a cytokine TNF inhibiting amount of an amide derivative of the Formula I, or a pharmaceutically-acceptable salt or in-vivo cleavable ester thereof, according to claim 1.

Claim 13 (new): A method for treating a disease or medical condition mediated by the production or effect of IL-1, IL-6 or IL-8, said method comprising administering to a warm-blooded animal in need thereof an IL-1, IL-6 or IL-8 inhibiting amount of an amide derivative of the Formula I, or a pharmaceutically-acceptable salt or <u>in-vivo</u> cleavable ester thereof, according to claim 1.

10